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Physical activity, intake of iron and folic acid with the risk of preeclampsia

Aktivitas fisik, asupan besi dan asam folat dengan resiko terjadinya preeklamsia

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Abstract

Preeclampsia (PE) is a health problem that often occurs during pregnancy. Pregnant women with preeclampsia are at risk for premature delivery, babies born with LBW, and increased maternal and infant mortality. This study aimed to measure the effect of physical activity and iron and folic acid intake on the risk of preeclampsia in pregnant women. A cross-sectional study was conducted in the Tangerang Regency in July 2022. 130 pregnant women aged ≥ 20 weeks were obtained using multistage sampling. Data were collected using the SQ-FFQ (the Semi-quantitative Food Frequency) Questionnaire (SQ-FFQ) and Physical Activity using a validated PAL (physical activity level) questionnaire. Data analysis was performed using Spearman's rank and Multiple Linear Regression tests. Results: There was an association between iron and folic acid micronutrient intake and preeclampsia incidence in pregnant women ($p<0,05$). Furthermore, simultaneous physical activity and iron and folic acid intake increased the risk of preeclampsia in pregnant women ($p<0,05$) by 10,7%. In conclusion, lack of physical activity and consumption of nutritious foods, especially those containing iron and folic acid, can increase the risk of preeclampsia during pregnancy.
Keywords: Pregnancy, micronutrients, exercise

Abstrak

Preeklamsia merupakan masalah kesehatan yang sering terjadi saat kehamilan. Wanita hamil dengan preeklampsia beresiko melahirkan prematur, bayi lahir dengan BBLR hingga peningkatan kematian ibu dan bayi. Tujuan penelitian untuk mengukur pengaruh aktivitas fisik, asupan besi dan asam folat dengan resiko terjadinya preeklampsia pada wanita hamil. Desain penelitian *cross sectional,* telah dilakukan di Kabupaten Tangerang, pada Juli 2022. Sampel yaitu ibu hamil berusia kehamilan ≥ 20 minggu sebanyak 130 orang diambil menggunakan *multistage sampling*. Pengumpulan data asupan menggunakan kuesioner SQ-FFQ (*Semi quantitative Food frequency*) dan aktivitas fisik menggunakan kuesioner PAL (*Physical Activity level*) yang telah divalidasi. Analisis data menggunakan uji *Rank Spearman* dan uji regresi linier berganda. Hasil, terdapat hubungan antara asupan mikronutrien zat besi dan asam folat dengan kejadian preeklamsia pada ibu hamil ($p<0,05$). Selanjutnya, secara simultan aktivitas fisik, asupan besi dan asam folat berpengaruh terhadap resiko terjadinya preeklamsia pada ibu hamil ($p<0,05$) sebesar 10,7%. Kesimpulan, kurangnya melakukan aktivitas fisik dan kurang mengkonsumsi makanan bergizi terutama yang mengandung zat besi dan asam folat dapat meningkatkan resiko mengalami preeklampsia selama kehamilan.
Kata Kunci: Kehamilan, mikronutrien, olahraga

Introduction

Preeclampsia is a disorder experienced during pregnancy characterized by a de novo progression of hypertension and proteinuria simultaneously, which develops into multiorgan dysfunction and is associated with an increased risk of cardiovascular and metabolic diseases later in life. Preeclampsia can complicate more than 5% of pregnancies (Christiansen et al., 2022).

Preeclampsia is one of several health problems that exist during pregnancy and has the potential for complications in 2-3% of pregnancies (Sukmariah et al., 2019). Preeclampsia is a serious medical condition that affects 3–5% of pregnancies, contributing to more than 35.000 maternal deaths worldwide each year. Preeclampsia can affect the work of other organs, causing an increased risk of complications in pregnancy (Wen et al., 2018).

According to the World Health Organization (WHO), the prevalence of preeclampsia in developing countries is seven times higher than in developed countries. The prevalence of preeclampsia ranges from 1,3 to 6% in developed countries and 1,8 to 18% in developing countries. The World Health Organization reports that preeclampsia contributes to 70.000 maternal deaths each year worldwide (Arikah et al., 2021). Health profile data shows an increase in maternal mortality cases in Indonesia, from 4.221 deaths in 2019 to 4.726 deaths in 2020. The main factors contributing to high maternal mortality include 25% due to bleeding (1.330 cases), 24% have hypertension in pregnancy, including preeclampsia and PEB, with 1.110 cases, and 8% have disorders of the circulatory system in 230 cases (Kementerian Kesehatan RI, 2020). The maternal mortality rate in 2017 was 43 cases and increased to 44 cases in 2018. Tangerang Province health profile data in 2018 explains that maternal death cases are caused by preeclampsia, and eclampsia amounted to 54% (24 cases) of all maternal deaths. In 2021, there were 35 cases of preeclampsia in pregnant women and 81 cases of preeclampsia in maternity women (Dinkes Kabupaten Tangerang, 2018; Aulya et al., 2021).

Gestational hypertensive disorders, including preeclampsia, are one of the leading causes of maternal morbidity and mortality. Women who exercise as recommended have a 30% lower risk of developing gestational hypertensive disorders (Witvrouwen et al., 2020).

Some preventive efforts that can be made for the prevention of preeclampsia in pregnant women include paying attention to food intake during pregnancy and doing physical activity. Pregnant women who do moderate to heavy physical activity can reduce the risk of preeclampsia and hypertension in pregnancy, with the aim of controlling weight gain during pregnancy. A study shows that women who engage in high levels of physical activity before pregnancy and continue during pregnancy are less likely to experience preeclampsia than women with low physical activity or a sedentary lifestyle (David et al., 2016). Exercise during pregnancy can reduce oxidative stress so as to improve endothelial function and, in theory, can reduce the risk of preeclampsia. Exercise is recommended for a duration of 30–60 minutes, which is done regularly 2–7 times a week (Malosso et al., 2017).

In addition to physical activity, pregnant women should consume a variety of foods. Adequate intake of micronutrients before and during pregnancy has an important role in maternal and fetal health. The need for folic acid during pregnancy affects the formation of cells and the nervous system, including red blood cells. Sources of folic acid include green vegetables and legumes that are high in folic acid (Kementerian Kesehatan RI, 2014). The recommended requirement for folic acid during pregnancy based on RDA is 1,3 mg for women aged 19–49 years and an additional 0.6 mg during pregnancy (Kementerian Kesehatan RI, 2019). The World Health Organization recommends taking oral iron supplements for pregnant women (30–60 mg of iron and 400 mg of folic acid) for six months in countries with a prevalence of anemia of 40% and an additional three months in countries with a prevalence of anemia > 40%. The addition of iron supplements and folic acid can prevent preeclampsia during pregnancy (Klemm et al., 2020; Adaji et al., 2019).

Multivitamins containing folic acid can reduce the risk of hypertension in pregnancy by 38%. Daily folic acid supplementation of 0,2 mg and 5 mg has the effect of reducing the risk of preeclampsia. Some research evidence explains

that the consumption of folic acid supplements with an average dose of 5,6 mg/day provides a protective effect against the effects of birth due to preeclampsia in low-birth-weight babies and premature babies (Singh et al., 2015). In contrast to a study explaining that consumption of folic acid supplementation as much as 4,0 mg/day after the first trimester does not prevent preeclampsia in high-risk women (Wen et al., 2018).

Research on preeclampsia has indeed been found, but physical activity factors and nutritional intake of iron and folic acid, which are seen simultaneously as risk factors for preeclampsia, have not been widely studied. Thus, the purpose of this study was to determine the relationship between physical activity, iron intake, and folic acid and the risk of preeclampsia in pregnant women in the Tangerang area.

The novelty of the study was to see the association of lack of physical activity, folic acid intake, and iron acid simultaneously with the incidence of preeclampsia in pregnancy. See the adequacy of iron and folic acid in foods consumed every day during pregnancy. It is hoped that this study will provide empirical evidence as an early intervention to prevent preeclampsia in pregnant women and will be one of the early screening methods for preeclampsia prevention carried out by health workers in first-level health facilities.

Methods

This study is an analytical study using observational research and a cross-sectional research design. Cross-sectional research is a study conducted in conjunction with exposure and observation (Probandari et al., 2020). The population is all pregnant women domiciled in Tangerang Regency. Sampling using multistage sampling in accordance with the criteria set by researchers obtained 130 samples of pregnant women with gestation ≥ 20 weeks. Data collection was conducted in July 2022.

The research data included respondents' characteristics (gestational age, parity, age, blood pressure, diagnosis). Data on gestational age, parity, and age of respondents were obtained from MCH books, and blood pressure data were obtained from conducting blood pressure checks conducted by Public Health Center (PHC) midwives. Nutrient intake data were obtained through interviews using semi-quantitative food frequency (FQ-FFQ) and food recall questionnaires, while physical activity data were obtained through interviews using Physical Activity Level (PAL) questionnaires. The study subjects signed informed consent before the interview.

Univariate analysis using frequency distribution was used to see a picture of the research variables used, including respondents' age, gestation, blood pressure, physical activity categories, and intake of micronutrients (iron and folic acid). Age grouping refers to the requirements that pregnant women should not be too young (< 18 years) or too old (>35 years), gestation based on trimester of pregnancy, blood pressure based on WHO, where normal blood pressure is 120/80 mmHg, physical activity based on grouping using the Physical Activity Level (PAL) questionnaire, and nutrient intake based on the Recommended Dietary Allowances (RDA).

Bivariate analysis was used to see the correlation between independent variables and dependent variables, which included the correlation of physical activity with preeclampsia, the correlation of adequacy of iron intake with preeclampsia, and the correlation of adequacy of folic acid intake with preeclampsia. The Kolmogorov-Smirnov test is used to determine the distribution of data, from which non-normally distributed data with p values <0,05 are obtained. The analysis test used if the data is not normally distributed is the Spearman rank with an α= 0,05.

Multivariate analysis shows the closeness of the relationship between the independent variable and the dependent variable. The statistical test used in this study is multiple linear regression, which measures how strong the relationship is between each independent variable and the dependent variable (Sumardiono et al., 2020). Multiple linear regression tests are used to test the effect of physical activity variables, iron intake, and folic acid on the risk of preeclampsia in pregnant women. A significant p ≤ 0,05 was used to test the hypothesis.

The method used in this study has been approved by the Health Research Ethics Committee, Faculty of Medicine, Sebelas Maret University Surakarta, based on the letter of the Ethics Committee with No. 35/UN27.06.11/KEP/EC/2022 on April 4, 2022.

Result and Discussion

Characteristics of research responses

The respondents of this study were pregnant women domiciled in Tangerang Regency with a gestational age of ≥ 20 weeks. In Table 1, you can see an overview of the characteristics of respondents.

Table 1. Characteristics of respondents (n= 130)

Characteristic	n	%
Age		
Risk (<18 y.o)	41	31
Productive (>35 y.o)	89	68
Parity		
Risk (> 3 child)	26	20
No risk (≤ 3 child)	104	80
Gestation		
2nd trimester (22-28 weeks)	61	46,9
3rd trimester (29-42 weeks)	69	53,1
Blood pressure		
Hypertension (>120/80 mmHg)	67	51,5
Usual (120/80 mmHg)	63	48,5
Physical activity (PAL)		
Light (1,4-1,69)	10	7,7
Keep (1,77-1,99)	25	19,2
Heavy (2-2,4)	95	73,1
Iron intake		
Less (< 80% RDA)	21	16,2
Enough (≥ 80% RDA)	109	83,8
Folic acid intake		
Less (< 80% RDA)	111	85,4
Enough (≥ 80% RDA)	19	14,6

Table 1 shows the characteristics of respondents in the study, including respondents with productive age (20–35 years) as much as 68,5%, parity (1-2 children) with live birth as much as 80%, gestational age (gestation) of 21–36 weeks as much as 53,1%, and hypertension as much as 51,5%. For physical activity, most pregnant women do physical activity with a weight category of as much as 73,1%. Iron micronutrient intake in pregnant women is mostly sufficient as needed, which is 83,8%, and folic acid micronutrient intake is still in the lower category of 85,4%.

Association of Physical Activity, Iron and Folic Acid Adequacy with the Incidence of Preeclampsia

Table 2 shows the results of the relationship between physical activity, iron adequacy, and folic acid intake using the Spearman Rank test.

Table 2. Relationships between variables

Variable	n	p-value	r-value
Physical activity with preeclampsia	130	0,228	0,106
Iron intake with preeclampsia	130	0,037	0,183
Folic acid intake with preeclampsia	130	0,002	0,266

In Table 2, there are results that show no relationship between physical activity and the incidence of preeclampsia, where the correlation value (r) is 0,106 (p = 0,228) and p >0,05. There is a relationship between iron nutrient adequacy and the incidence of preeclampsia, with a value of r = 0,183 (p = 0,037) p < 0,05. The strength of the association is very weak, where the variable iron nutrient intake can explain the incidence of preeclampsia in pregnant women by 3,35% and 96,65% explained by other variables outside the study.

The variable folic acid showed a correlation between folic acid adequacy and the risk of preeclampsia with a correlation value (r) 0,266 (p = 0,002) p <0,05. The strength of the relationship is sufficient, where the variable intake of folic acid nutrients can explain the incidence of preeclampsia in pregnant women by 7,1% and 92,9%, respectively, explained by other variables outside the study.

The Simultaneous Association of Physical Activity and Nutritional Intake with the Risk of Preeclampsia

Table 3 describes the results of statistical analysis using multiple linear regression to see the simultaneous relationship of physical activity, iron, and folic acid intake with the risk of preeclampsia during pregnancy.

When viewed in Table 3, independently, physical activity and iron intake did not affect the incidence of preeclampsia with a significant value (p > 0,05), while folic acid intake affected the incidence of preeclampsia. Based on significant values of F (0,011) < 0,05 (p < 0,05), it was concluded simultaneously that physical activity, adequacy of iron intake, and folic acid influenced the occurrence of preeclampsia by 8,5%, while 91,5% were influenced by other factors outside the study.

The characteristics of respondents are mostly pregnant women who experience preeclampsia with high blood pressure at the

age of 20–35 years, gestational age of 21–36 weeks, and parity of 1-2 children. Preeclampsia is gestational hypertension with proteinuria or end-organ dysfunction. The cause of preeclampsia is not known for sure. Here are some risk factors associated with the development of preeclampsia, including extreme age (too young or too old), parity, previous history of preeclampsia, pregnancy spacing, IVF, family history of preeclampsia, obesity, having a comorbid medical history including gestational diabetes, previous chronic hypertension, kidney disease, and autoimmune disorders including systemic lupus erythematosus and syndrome antiphospholipid (Poon et al., 2019).

Table 3. Relationships between variables simultaneously

Variable	Unstandardized Coefficient		Standardized Coefficient	t	p-value
	B	Std. eror	Beta		
(Constant)	1,312	0,274	0,012	4,792	0,000
Physical activity	0,010	0,069		0,142	0,888
Iron intake	-0,018		-0,032		
Folic acid intake	0,156	0,048		-0,370	0,712
R square	0,085		0,283		
F	3,900	0,048		3,251	0,001
Sig. F	0,011				

This study suggests that simultaneously, the risk of preeclampsia can be caused by a lack of physical activity and insufficient dietary intake, such as insufficient consumption of foods rich in iron and folic acid during pregnancy. Gestational hypertensive disorders, including preeclampsia, are the main cause of MMR and AKB. Women who exercise as recommended have a 30% lower risk of developing gestational hypertensive disorders (Witvrouwen et al., 2020).

Malosso et al. (2017) describe a meta-analysis of 17 randomized studies involving 5,075 pregnant women < 23 weeks gestation. All of these studies looked at early pregnancy physical activity (aerobic exercise for 30–60 minutes, 2–7 times per week) associated with a lower prevalence of hypertension during pregnancy (RR = 0,70, 95% CI 0,53–0,83; 7 studies, n = 2,517). These pregnant women had a much lower risk of gestational hypertension (RR = 0,54, 95% CI 0,40-0,74; 16 studies, n = 4,641) compared with pregnant women in the control group.

However, researchers do not mention the importance of exercise to prevent preeclampsia. Incidence of preeclampsia in pregnant women who did aerobic exercise (without dietary counseling) and pregnant women who did not exercise (RR = 0,79, 95% CI 0,45-1,38; 6 studies, n = 2,230) (Malosso et al., 2017; Poniedziałek-Czajkowska et al., 2023).

Physical activity before or during pregnancy can have an impact on changes in body functions that ultimately lead to preeclampsia. This has an effect on placental development, reduction of oxidative stress, and pro-survival response, which is considered to play an important role in maintaining or improving endothelial function. Physical exercise can have a good effect on the function of these organs by controlling body weight and reducing hormonally active adipose tissue, which can reverse metabolic abnormalities typical of obesity. In addition, it can normalize placental angiotensin II type 1 and modulate the function of the RAA (Renin-Angiotensin) system, which results in inhibiting the development of preeclampsia (Poniedziałek-Czajkowska et al., 2023).

A TOP-mums study concluded that there is a relationship between lifestyle deviations affecting maternal metabolism and placental function in the first trimester of pregnancy. The recommended intervention for the prevention of complications is to promote a healthy lifestyle, starting in the early phase of preconception, as a first step to overcoming chronic diseases and stopping the decline of unhealthy lifestyles in the next generation (Timmermans et al., 2019).

Women during pregnancy experience an increased intake of nutrients to support the health and development of the fetus. In addition to macronutrient intake, micronutrient intake is also necessary for fetal development in the womb. In this study, a correlation was obtained

between the adequacy of folic acid and iron micronutrient intake and the incidence of preeclampsia.

A different study conducted by Alvestad et al. (2022) is a cohort study involving 100,105 pregnant women in Norway who have epilepsy and do not have epilepsy. The study concluded that folic acid was not associated with the risk of preeclampsia in pregnant women with epilepsy. Folic acid plays an important role in DNA synthesis, so there will be an increased need during pregnancy due to the growth of the uterus, placenta, and fetus. Folic acid deficiency can result in poor implantation and vascularization of the placenta and then premature birth, preeclampsia, fetal growth retardation, and other placenta-related pregnancy complications (Alvestad et al., 2022; Li et al., 2019).

Women should take a multivitamin containing folic acid when planning a pregnancy and entering early pregnancy for primary prevention of neural tube damage and other possible congenital anomalies. A study conducted by Liu et al. (2018) on the relationship between folic acid supplements and the risk of preeclampsia showed that multivitamin supplements containing folic acid significantly reduced the risk of preeclampsia, while folic acid supplementation alone did not have a significant effect on the risk of preeclampsia. Folic acid supplements may reduce the risk of preeclampsia. It is thought that folic acid may reduce levels of hyperhomocysteinemia, which can damage the vascular endothelium of the developing placenta. Folic acid deficiency can induce apoptosis of cytotrophoblastic cells and possibly affect trophoblastic invasion and placental development, so folate supplementation may address the underlying metabolic effects of folate metabolism in women at risk for preeclampsia (Liu et al., 2018).

A folic acid intake of 3,1 mg/kg body weight per day can meet nutritional needs, but pregnant and lactating women need a folic acid intake of 0,4 mg/day, which affects fetal development. Folic acid deficiency can result in megaloblastic anemia. Some of the causes of folic acid deficiency are extreme diet, serious illness, vitamin C deficiency, excessive vomiting, hemolytic anemia, and the use of anticonvulsants, as well as alcohol consumption. Symptoms of folate deficiency include fatigue, weakness, dyspnea, edema, loss of appetite, diarrhea, depression, and nausea (Lazulfa, 2019).

During pregnancy, the increased need for iron is useful for the formation of new cells and tissues. The World Health Organization recommends taking oral iron supplements for pregnant women (30–60 mg of iron and 400 mg of folic acid) for six months in countries with a prevalence of anemia of 40% and an additional 3 months in countries with a prevalence of anemia > 40%. Regular consumption of iron supplements has been shown to prevent anemia and complications in pregnancy (Mardhiah & Marlina, 2019). Research conducted on anemic pregnant women shows the results of the influence of iron intake on the decrease in the incidence of anemia in pregnant women (Arman & Sumiaty, 2022). A study conducted in Nigeria explained that there was no difference between giving supplements twice a day and once a day in serum ferritin in pregnant women, but there was a significant difference in adherence to taking iron supplements once a day (65 mg) in pregnant women and lower side effects (Adaji et al., 2019).

Hemoglobin deficiency results in anemia. Babies are born with a low birth weight, which increases the risk of bleeding and death. Some sources of iron are foods such as fish, chicken, beef, eggs, liver, tempeh, nuts, and green vegetables. It is recommended to consume blood-added tablets during pregnancy once per day to meet iron needs during pregnancy. The recommended iron intake during pregnancy based on RDA is 18 mg in the first trimester, and there is an additional need in the second and third trimesters of 9 mg (Kementerian Kesehatan RI, 2019).

The limitations of this study were that the sample size of pregnant women with preeclampsia was limited, and food intake was not measured to the metabolic equivalent of various activities because here the researchers only looked at overall physical activity. Further research is expected to be carried out to arrive at the calculation of metabolic equivalents for each activity carried out.

Conclusion

Lack of physical activity during pregnancy or sedentary lifestyle and lack of intake of micronutrients folic acid and iron can simultaneously be significantly associated with the risk of preeclampsia during pregnancy.

To prevent preeclampsia, it is recommended to consume a variety of foods, especially those containing iron and folic acid, and do regular exercise for 30–60 minutes with a frequency of 5-7 times a week. Check pregnancy regularly with health workers to determine the health of the mother and fetal development to avoid complications during pregnancy.

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